In item 2, the Office objected to the term "SEC DI No. 24" on page 4 of the specification. Applicants have amended the specification to change the term "SEC DI No. 24" to "SEQ ID NO: 24," and request that this objection be withdrawn. Minor grammatical changes were also made to the paragraph containing this term, which do not add new matter.

In item 3, the Office rejected claims 57-59 under 35 U.S.C. § 112, second paragraph, for being vague and indefinite. References to a non-elected invention were cited in this rejection. Claims 57-59 have been cancelled and new claims 65-80 are provided, which address each point of this rejection.

Specifically, in item 4, the Office asserted that the form of the claims should reflect the election. New claims 65 and 70 begin with "[a] porcine vaccine against a pathogen of interest, wherein the vaccine comprises a helper virus, a recombinant virion, and a pharmaceutical excipient;" new claim 69 begins with "[a] porcine vaccine against *Mycoplasma hyopneumoniae*, wherein the vaccine comprises a helper virus, at least one recombinant virion, and a pharmaceutical excipient, wherein the recombinant virion(s) comprises;" new claims 73 and 78 begin with "[a] porcine vaccine against a pathogen of interest, wherein the vaccine comprises at least one recombinant virion and a pharmaceutical excipient, wherein the recombinant virion(s) is prepared according to the method comprising;" and new claim 77 begins with "[a] porcine vaccine against *Mycoplasma hyopneumoniae*, wherein the vaccine comprises at least one recombinant virion and a pharmaceutical excipient, wherein the recombinant virion(s) is prepared according to the method comprising, ..." The claims continue with the characteristics

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of the virion or method of preparation of the virion. Therefore, the amended claims are definite and refer to the elected invention of a porcine vaccine.

In item 4, the Office also asserted that the reference to an "infectious agent having tropism for mucoses," was vague and indefinite. The new claims do not contain this language and therefore obviate the rejection.

In addition, the Office asserted that the components of the vaccine were not provided. New independent claims 65, 69, 70, 73, 77, and 78 provide components of the claimed vaccine by providing characteristics of the TGEV genome that comprise the recombinant virus in the claimed vaccine. New claims 70 and 74 also provide that these features of the TGEV genome are expressed from a plasmid as a recombinant RNA. This RNA is then transfected into cells, which have previously been infected with a helper virus, to produce the recombinant virions that can be used as a vaccine. Therefore, the new claims are not vague, but definitively claim the invention.

Because the new claims are definite and clearly define the invention, Applicants respectfully request that the rejection under 35 U.S.C.§ 112, second paragraph, be withdrawn.

In items 3 and 4 on page 4, the Office also rejected the claims under 35 U.S.C. § 112, first paragraph, because it was asserted that the specification did not enable a skilled artisan to make or use the invention. The new claims are enabled by the specification and meet the requirements of 35 U.S.C. § 112, first paragraph, as identified in points 1 through 3 by the Office.

In point 1, the Office asserted that guidance for preparing a suitable expression vector was not provided. The new claims recite characteristics of a recombinant virion

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used in the claimed vaccine. These include at least 1.9 kb of the 5' end of a TGEV genome (supported in Example 1, section 1.4.1, page 16, lines 11-13 and Table 2 of the specification), the pseudoknot region of the TGEV genome, including the region of overlap between ORFs 1a and 1b, of the TGEV genome (supported in Example 1, section 1.4.5, page 18, lines 30-41 of the specification), incomplete S, M, and N structural genes (supported in Example 1, section 1.2.1, page 13, lines 27-31 of the specification), the 3' end of the gene, from bp 9691-9707 (supported in Example 1, section 1.2.1, page 13, lines 25-27 and Table 2 of the specification), and a heterologous gene under the control of the S gene promoter (supported by Example 2).

A method of preparing the claimed vaccine, by constructing a recombinant plasmid comprising a heterologous gene and the recited genomic elements indicated, producing RNA by transcribing this plasmid, introducing the RNA produced from the plasmid into cells infected with helper virus, and producing recombinant virion, is provided in new claims 73, 77, and 78. This method is supported by Example 2 of the specification. Therefore, the new claims provide adequate guidance for preparation of the claimed invention as expression vectors and systems or vaccines.

In point 2, the Office asserted that many DI particles are not suitable expression vectors, and that portions of the genome required for construction of a suitable expression vector should be provided. The Office provides no support, though, for its statement that DI particles are not suitable expression vectors, other than the background in the specification describing the field of the invention.

As discussed above, the new claims recite portions of the TGEV genome. Use of these portions of the genome, as DI particles, is demonstrated in Examples 3 and 5.

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Specifically, Example 3.1 describes experiments in which the claimed vaccine was used to immunize pigs and "total protection was provided against infection by PEDV (strain SEG86-1) . . . ." (Specification, page 20, lines 39-40.) In Example 3.3 "total protection was provided against infection by PRRSV (strain Fort Dodge) in 10-day-old piglets . . . ." (Specification, page 21, lines 18-19.) Additionally, in Example 3.2 immunization of dogs with a vaccine, similar to the claimed vaccine in pigs, was used and "the presence of antibodies specific to canine coronavirus was determined using RIA." (Specification page 21, lines 2-3.) In addition, Example 5 describes the expression of recombinant monoclonal antibody 6A.C3 in pigs. The results showed that "[t]he recombinant antibodies had RIA titers higher than 10^3 and are able to reduce the titer of the infectious virus more than 10^4 fold." (Specification page 22, lines 17-18.)

As held in *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1971):

> As a matter of Patent Office practice . . . a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Id. at 223, 169 U.S.P.Q. at 369 (emphasis in original). Therefore, in the absence of some showing of a reason to doubt the statements in the specification, a suitable expression vector as claimed was demonstrated and has been enabled.

In point 3, the Office asserted that only two working embodiments were provided and that guidance to making or using other suitable constructs was not provided. Applicants assert that the analysis of the common genomic features provided in the specification, for instance in Example 1 at sections 1.4.4 and 1.4.5, on pages 17-19 of

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the specification, provide sufficient guidance as to the regions of the genome that will produce suitable vaccines as claimed.

Finally, in point 4, the Office asserted that the claims were of excessive breadth and not supported by the disclosure. While Applicants courteously disagree with the Office's assertion, Applicants point out that the new claims are directed to a porcine vaccine, which is supported by the disclosure in Examples 3, 4, and 5.

Because the new claims are enabled by the specification for making and using a porcine vaccine from recombinant virions, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

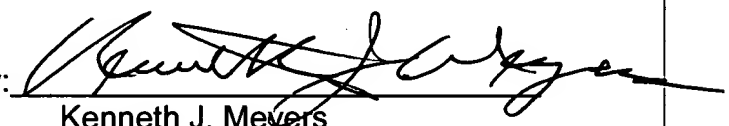
In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: July 18, 2002

By: 

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Appendix to the Amendment of July 18, 2002

Please amend the paragraph bridging pages 4 and 5 as follows:

Figure 12 shows the complete RNA DI-C cDNA sequence [(see SEC. DI No. 24)] (See SEQ ID NO: 24) obtained by the sequencing of overlapping fragments of the *a, b, c*, and *d* cloning. RNA DI-C has kept four discontinuous parental genome regions: I, II, III and IV. The flanking sites of these regions are indicated with arrows. The translation of the three ORFs present in genome DI-C is indicated: chimeric ORF of 6.7 kb resulting from the fusion of discontinuous regions I and II in phase; the mini-ORF of three amino acids preceding it in phase[,]; and the ORF, which initiates [in] at the AUG of gene S. Highly homologous regions -- with the proteic domains described for other coronaviruses as those responsible for the polymerase and helicase activities, and metal ion binding sites -- appear shaded. CTAAAC transcription promoter sequences appear shaded. The overlapping area between ORFs 1a and 1b (41 nucleotides) appears shaded, the slippery sequence of the ribosome [appears] is underlined, and the ORF1a termination codon is in a box. In positions 637, 6397, and 6485, the specific changes with respect to the parental genome are indicated. The nucleotides present in the parental genome in these positions are indicated.

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